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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CLARK, AMY LYNN	
ART UNIT	**PAPER NUMBER**
1655	

DATE MAILED: 08/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/525,992	ARORA ET AL.	
	Examiner	Art Unit	
	Amy L. Clark	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *5-8 and 12-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/28/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Acknowledgment is made of the receipt and entry of the amendment filed on 30 May 2006 with the amendment of Claims 1-19 and newly added Claim 20.

Applicant's election with traverse of Group I, Claims 1-11 in the reply filed on 30 May 2006 is acknowledged. The traversal is on the grounds that the newly amended claim 1, which recites "An anticonvulsant pharmaceutical composition for nasal administration having binding affinity...consisting essentially of 1.) an extract of the pericarp of the fruit of *S. trifoliatus*, comprising from 0.001 to 1%w/v of hederagenin and at least one pharmaceutically acceptable additive" now excludes from the claimed composition extract from plants other than *S. trifoliatus*. Applicant further argues that the composition disclosed in Gupta et al. (N*) requires an extract from *Emblica officinalis* to provide a synergistic effect with an extract from *S. trifoliatus*. Applicant further argues that the specification of the present application, the composition disclosed in Gupta is associated with the following shortcomings, it involves two active principals, it involves a lengthy extraction, it uses nitrogen gas throughout the period of soaking and extracting, it uses a number of pharmaceutically acceptable additives and uses alum, which is a known irritant and a corrosive chemical in the composition and therefore, will require more manufacturing time, which is not cost effective, and is less safe. Applicant further argues that on page 9 of the specification of the current invention that there "exists a need, therefore, for a method of treatment of migrane which addresses the shortcomings of the existing methods and which, moreover, is

safe, less expensive and is convenient, which forms the objective of the present invention". Applicant further argues that in view of the foregoing, that it is respectfully submitted that claim 1 is patentable over Gupta et al. and therefore, there is a unity of invention. Applicant further argues Gupta does not teach 0.001 to 1% w/v of hederagenin present in the extract that is combined wither at least one pharmaceutically acceptable additive to form the compositions claimed in Claim 1. Applicant further argues that they have discovered a novel and non-obvious composition for nasal administration that does not require and extract from a plant other than *S. trifoliatus* and in which the extract has a specific concentration of 0.001 to 1.0% w/v of hederagenin and in combination with at least one pharmaceutically acceptable additive forms the composition for nasal administration. Applicant further argues that in view of the foregoing, Applicant's respectfully submit that pending Claims 1-11 are in condition for allowance and the restriction requirements should be withdrawn. Applicant further argues that MPEP 1850 states, "If the independent claims avoid the prior art and satisfy the requirement for unity of invention, no problem of lack of unity arises in respect to any claims that depend on the independent claim" and that the MPEP also states, "The method for determining unity of invention under PCT Rule 13 shall be construed as permitting , in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application: (A) in addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product;..." Applicant further argues that there was no lack of unity found by the European Patent Office in the corresponding PCT

application. This is not found persuasive for the reasons set forth in the previous Office Action and for the reasons set forth below.

The special technical feature of Group I is drawn to an anticonvulsant pharmaceutical composition for nasal administration having binding affinities for the receptor sites viz. GABA-A agonist site, Glutamate- AMPA site, Glutamate-Kainate site, Glutamate-NMDA agonistic site, Glutamate-NMDA glycine (Strychnine insensitive) site and Sodium channel (site 2) comprising an extract of the pericarp of the fruit of *S. trifoliatus*, comprising from 0.001 to 1.0 (%w/v) of hederagenin and pharmaceutically acceptable additives. The special technical feature of Group II is a process for preparation of an extract containing 4 to 8% w/w of hederagenin comprising the steps of extraction of the pericarp of the fruit of *S. trifoliatus* with water or an alcohol or a mixture thereof at ambient to boiling temperature of 0.5 to 24 hours, lyophilization of the aqueous, alcoholic or aqueous alcoholic extract containing a mixture of saponins to give a lyophilized powder containing a mixture of saponins and reconstitution of the lyophilized extract in water to achieve a concentration of hederagenin between 0.001 to 1.0 (% w/v), which is not required for Group I. The special technical feature of Group III is a process for preparation of an anticonvulsant pharmaceutical composition comprising adding lyophilized aqueous extract of *S. trifoliatus* as claimed in claim 12 to a mixture of chlorobutaol and phenylethyl alcohol in water and sodium chloride to get a uniform dispersion, filtering, mixting above dispersion with dispersion of xanthan gum in purified water and adjusting the pH between 4.5 to 6.5, which is not required for Group I. The special technical feature of Group IV is an extract according to Claim 1, which

exhibits in vitro receptor binding affinity towards specific receptors like GABA-A agonistic site, Glutamate- AMPA site, Glutamate-Kainate site, Glutamate-NMDA agonistic site, Glutamate-NMDA glycine (Strychnine insensitive) site and Sodium channel (site 2) which have mediatory role in anticonvulsant effect, which is not required for Group I. Finally, Claim 1, at least, is anticipated by or obvious over Gupta et al. (CA2409051, 29.11.2001). Gupta teaches a pharmaceutical composition for treating migrane comprising of an extract of the pericarp of the fruit of *Sapindus trifoliatus* in an amount of 0.1 to 1.0 % w/v (See page 11, lines 1-14 and page 38, claim 1) and pharmaceutically acceptable additives in the form of nasal drops (See Abstract). Gupta further teaches that *Sapindus trifoliatus* inherently contains hedergenin (See page 11, lines 10-13). Gupta does not specifically teach a composition having binding affinities for the receptor sites viz. GABA-A agonist site, Glutamate- AMPA site, Glutamate-Kainate site, Glutamate-NMDA agonistic site, Glutamate-NMDA glycine (Strychnine insensitive) site and Sodium channel (site 2) nor does Gupta specifically teach 0.001 to 1.0 (%w/v) of hederagenin present in the composition, however, the composition as taught by Gupta has the same functional effect as the composition claimed by Applicant. Consequently, the special technical feature which links the claims does not provide a contribution over the prior art, so the invention lacks unity.

In response to Applicant's argument that the amendment of Claim 1 now excludes from the claimed composition extract from plants other than *S: trifoliatus*, please note the following:

MPEP 211.03 states,

"If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. *In re De Lajarte*, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also *Ex parte Hoffman*, 12 USPQ2d 1061, 106364 (Bd. Pat. App. & Inter. 1989) ("Although 'consisting essentially of' is typically used and defined in the context of compositions of matter, we find nothing intrinsically wrong with the use of such language as a modifier of method steps. . . [rendering] the claim open only for the inclusion of steps which do not materially affect the basic and novel characteristics of the claimed method. To determine the steps included versus excluded the claim must be read in light of the specification. . . . [I]t is an applicant's burden to establish that a step practiced in a prior art method is excluded from his claims by 'consisting essentially of' language)."

In response to Applicant's argument that the composition disclosed in Gupta is associated with the following shortcomings, it involves two active principals, it involves a lengthy extraction, it uses nitrogen gas throughout the period of soaking and extracting, it uses a number of pharmaceutically acceptable additives and uses alum, which is a known irritant and a corrosive chemical in the composition and therefore, will require more manufacturing time, which is not cost effective, and is less safe, please note that this argument is drawn to a product by process. Please note that in the case of a Product-by-Process, the process of producing the product is given no patentable weight since it does not impart novelty to a product when the product is taught by the prior art.

See *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983) and *In re Brown*, 173 USPQ 685 (CCPA 1972). Consequently, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product *per se*, even when limited to the particular process, is unpatentable over the same product taught in by the prior art. See *In re King*, 107 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); *In re Merz*, 97 F.2d 599, 601, 38 USPQ 143-145 (CCPA 1938); *In re Bergy*, 563 F.2d 1031, 1035, 195 USPQ 344, 348 (CCPA 1977) *vacated* 438 US 902 (1978); and *United States v. Ciba-Geigy Corp.*, 508 F. Supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979). Finally, since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional characteristics of the claimed composition and the composition of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

In response to Applicant's argument that there "exists a need, therefore, for a method of treatment of migrane which addresses the shortcomings of the existing methods and which, moreover, is safe, less expensive and is convenient, which forms the objective of the present invention", it is important to note that this a relative phrase. The terms "safe", "less expensive" and "convenient" are all relative terms and it is unclear as to what degree of difference Applicant's claimed composition would make. Please note that Gupta claims that a composition comprising an aqueous extract of *Sapindus trifoliatus* is safe and effective to use, without any harmful side effects and would particularly avoid/reduce chances of damage/irritation to the nasal mucosa

membrane when administered nasally and that an object of making a composition comprising an aqueous extract of *Sapindus trifoliatus* is to provide a process of manufacture of a formulation that is simple, specific and cost-effective (See page 13, lines 3-13). Therefore, it appears that Gupta is teaching that the same composition comprising an aqueous extract of *Sapindus trifoliatus* as Applicant and is teaching that the composition is safe, cost-effective and convenient.

In response to Applicant's argument that Gupta does not teach 0.001 to 1% w/v of hederagenin present in the extract that is combined wither at least one pharmaceutically acceptable additive to form the compositions claimed in Claim 1 and that Applicant has discovered a novel and non-obvious composition for nasal administration that does not require and extract from a plant other than *S. trifoliatus* and in which the extract has a specific concentration of 0.001 to 1.0% w/v of hederagenin and in combination with at least one pharmaceutically acceptable additive forms the composition for nasal administration, **evidence must be submitted to show that the claimed invention has unexpected results**. See MPEP 716.02-716.02 (g), but more specifically see the following:

MPEP 716.02, which states:

Any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986); *In re Waymouth*, 499 F.2d 1273, 1276, 182 USPQ 290, 293 (CCPA 1974); *In re Wagner*, 371 F.2d 877, 884, 152 USPQ 552, 560 (CCPA 1967); *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992).

MPEP 716.02 (c), which states,

"**Evidence of unexpected results must be weighed against evidence supporting *prima facie* obviousness in making a final determination of the obviousness of the claimed invention**. *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978)

Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of non-obviousness must be commensurate in scope with the claims which the evidence is offered to support." In other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range. *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980). See also *In re Peterson*, 315 F.3d 1325, 1329-31, 65 USPQ2d 1379, 1382-85 (Fed. Cir. 2003); *In re Grasselli*, 713 F.2d 731, 741, 218 USPQ 769, 777 (Fed. Cir. 1983); *In re Eli Lilly*, 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990)."

MPEP 716.02 (d), which states,

"Where the unexpected properties of a claimed invention are not shown to have a significance equal to or greater than the expected properties, the evidence of unexpected properties may not be sufficient to rebut the evidence of obviousness. *In re Nolan*, 553 F.2d 1261, 1267, 193 USPQ 641, 645 (CCPA 1977)

The nonobviousness of a broader claimed range can be supported by evidence based on unexpected results from testing a narrower range if one of ordinary skill in the art would be able to determine a trend in the exemplified data which would allow the artisan to reasonably extend the probative value thereof. *In re Kollman*, 595 F.2d 48, 201 USPQ 193 (CCPA 1979); *In re Lindner*, 457 F.2d 506, 509, 173 USPQ 356, 359 (CCPA 1972).

To establish unexpected results over a claimed range, applicants should compare a sufficient number of tests both inside and outside the claimed range to show the criticality of the claimed range. *In re Hill*, 284 F.2d 955, 128 USPQ 197 (CCPA 1960)."

In response to Applicant's argument that claim 1 is patentable over Gupta et al. and therefore, there is a unity of invention and Applicant's argument that MPEP 1850 states, "If the independent claims avoid the prior art and satisfy the requirement for unity of invention, no problem of lack of unity arises in respect to any claims that depend on the independent claim" and that the MPEP also states, "The method for determining

unity of invention under PCT Rule 13 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application: (A) in addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product;...", please note the following. Patentability is based upon novelty of an invention. Since it appears that Applicant is claiming the same invention as Gupta, Applicant's invention appears to lack novelty. Furthermore, lack of unity is determined by the following:

See MPEP 1850 (II):

"An international application should relate to only one invention or, if there is more than one invention, the inclusion of those inventions in one international application is only permitted if all inventions are so linked as to form a single general inventive concept (PCT Rule 13.1). With respect to a group of inventions claimed in an international application, unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" is defined in PCT Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art. The determination is made on the contents of the claims as interpreted in light of the description and drawings (if any).

Whether or not any particular technical feature makes a "contribution" over the prior art, and therefore constitutes a "special technical feature," should be considered with respect to novelty and inventive step. For example, a document discovered in the international search shows that there is a presumption of lack of novelty or inventive step in a main claim, so that there may be no technical relationship left over the prior art among the claimed inventions involving one or more of the same or corresponding special technical features, leaving two or more dependent claims without a single general inventive concept.

See also MPEP 1893.03(d):

"When making a lack of unity of invention requirement, the examiner must (1) list the different groups of claims and (2) explain why each group lacks unity with each

other group (i.e., why there is no single general inventive concept) specifically describing the unique special technical feature in each group".

The principles of unity of invention are used to determine the types of claimed subject matter and the combinations of claims to different categories of invention that are permitted to be included in a single international or national stage patent application. See MPEP § 1850 for a detailed discussion of Unity of Invention. The basic principle is that an application should relate to only one invention or, if there is more than one invention, that applicant would have a right to include in a single application only those inventions which are so linked as to form a single general inventive concept.

A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art. For example, a corresponding technical feature is exemplified by a key defined by certain claimed structural characteristics which correspond to the claimed features of a lock to be used with the claimed key."

Since there appears to be no contribution over the prior art, unity of the invention is, indeed, lacking.

In response to Applicant's argument that there was no lack of unity found by the European Patent Office in the corresponding PCT application, please note that the MPEP 1850 (I) states,

"Any international application must relate to one invention only or to a group of inventions so linked as to form a single general inventive concept (PCT Article 3(4)(iii) and 17(3)(a), PCT Rule 3.1, and 37 CFR 1.475). Observance of this requirement is checked by the International Searching Authority and may be relevant in the national (or regional) phase.

The decision in *Caterpillar Tractor Co. v. Commissioner of Patents and Trademarks*, >650 F.Supp. 218,< 231 USPQ 590 (E.D. Va. 1986) held that the Patent and Trademark Office interpretation of 37 CFR 1.141(b)(2) as applied to unity of invention determinations in international applications was not in accordance with the Patent Cooperation Treaty and its implementing regulations. In the Caterpillar international application, the USPTO acting as an International Searching Authority, had held lack of unity of invention between a set of claims directed to a process for forming a sprocket and a set of claims drawn to an apparatus (die) for forging a sprocket. The

court stated that it was an unreasonable interpretation to say that the expression "specifically designed" as found in former PCT Rule 13.2(ii) means that the process and apparatus have unity of invention if they can only be used with each other, as was set forth in MPEP § 806.05(e).

Therefore, when the Office considers international applications as an International Searching Authority, as an International Preliminary Examining Authority, and during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111. No change was made in restriction practice in United States national applications filed under 35 U.S.C. 111 outside the PCT."

Therefore, the Office determines whether there is lack of unity at the national stage regardless of whether the European Patent Office found a lack of unity.

Applicant further elected the following species: "lyophilized powder" from Claim 3, "tonicity" from Claim and nasal drops from Claim 11, with traverse. However, Applicant did not provide any grounds for traversal for the species election. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-9 and 12-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 1-20 are currently pending.

Claims 1-6, 10 and 11 are under examination.

Claim Objections

Claims 1-6, 10 and 11 are objected to because of the following informalities: Claim 1 contains the abbreviations, "GABA-A" in line 3, "AMPA" in line 3 and "NMDA" in line 4, which are neither defined in the claims nor in the specification. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of Claims 1-6, 10 and 11 are uncertain because it is unclear as to the identification of the ingredients to which Applicant intends to direct the subject matter particularly since it appears that Applicant is naming a genus and species of a plant, however, the genus of the plant needs to be written out completely since "*S. trifoliatus*" is not descriptive and is not defined in the claims. Claim 1 also recites the term "extract of the pericarp", however, Applicant does not specify what type of pericarp extract that is used. For example, is Applicant claiming a solvent extract or a biologically active compound obtained from the pericarp? The lack of clarity renders the claims indefinite since the resulting claims do not clearly set forth the metes and bounds of the patent protection desired.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta et al. (N*)

Gupta teaches a pharmaceutical composition for the prophylactic treatment of migranes comprising aqueous extracts of *Sapindus trifoliatus* pericap (See Abstract), which inherently contains hederagenin (See page 11, lines 10-13) in acidic conditions (please note that Gupta further teaches that the pH of the composition is maintained between 3.5 and 7.0, wherein a pH range between 3.5 and 5.5 is most preferred, See page 18, lines 20 and 21), which reads on an extract of the paricarp of the fruit of *Sapindus trifoliatus* comprising hederagenin and at least one pharmaceutically

acceptable additive. Gupta further teaches that the pharmaceutical composition further comprises an isotonic agent, such as sodium chloride (See page 19, lines 1 and 2), which reads on a tonicity agent. Gupta further teaches that the composition is obtained in the form of nasal drops (See Abstract) and that the fruit of *Sapindus trifoliatus* is used in the treatment of epilepsy (See page 11, lines 1-9), which reads on anticonvulsant. Please note that Gupta does not expressly teach that the composition has a binding affinity for at least one of the following selected from the group consisting of GABA-A agonist site, Glutamate-AMPA site, Glutamate-Kainate site, Glutamate-NMDA agonistic site, Glutamate-NMDA glycine (strychnine insensitive) site and sodium channel (site 2), however, the composition taught by Gupta is known to treat epilepsy, therefore, these properties are inherent to the composition taught by Gupta.

The teachings of Gupta are set forth above. Gupta does not expressly teach an anticonvulsant pharmaceutical composition for nasal administration comprising of an extract of the pericarp of *S. trifoliatus* comprising from 0.001 to 1.0 % w/v hederagenin nor does Gupta teach hederagenin in an amount from 0.004% of 0.08% w/v nor does Gupta teach that the extract is in the form of a lyophilized powder, nor does Gupta teach that the pH is in the range of between 4.5 and 6.5. However, at the time the invention was made, it would have been obvious to one of ordinary skill in the art and one would have been motivated and had a reasonable expectation of success to modify the amount of hederagenin in the composition taught by Gupta, to modify the form in which the extract of pericarp is in and to modify the pH of the composition, because at the time the invention was made, it was known that the paricarp of the fruit of *Sapindus trifoliatus*

inherently contained hederagenin, as clearly taught by Gupta. Furthermore, it would have been merely a matter of judicious selection to one of ordinary skill in the art at the time the invention was made to modify the referenced composition because it would have been well in the purview of one of ordinary skill in the art practicing the invention to pick and choose a concentration of hederagenin, it would have been well in the purview of one of ordinary skill in the art to choose a form that an extract was in, particularly since the extract was being made into a composition further comprising a pharmaceutically acceptable additive (please note that lyophilizing the extract simply makes the extract more concentrated since it is simply removing extraction solvent), and it would have been well in the purview of one of ordinary skill in the art to modify the pH of the composition to provide an anticonvulsant pharmaceutical composition for nasal administration and for prophylactic treatment of migrane comprising hederagenin, because at the time the invention was made, it was known in the art that the paricarp of the fruit of *Sapindus trifoliatus* inherently contained hederagenin and that it was useful for treating migranes and epilepsy, as clearly taught by Gupta. Thus, the claimed invention is no more than the routine optimization of a result effect variable.

The result-effective adjustment of particular conventional working conditions (e.g., modifying the amount of a bioactive compound in a composition, using a desired form of an extract, and adjusting the pH of a solution) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to add any of the claimed ingredients in the making of the claimed composition because it is well known that its *prima facie* obvious to combine two or more ingredients, each of which is taught by the prior art, to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. *In re Susi*, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); *In re Crocketti*, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960).

Based upon the beneficial teachings of the cited references, the skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy L. Clark whose telephone number is (571) 272-1310. The examiner can normally be reached on 8:30am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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